Appl. No. : **10/026,066**
Filed : **December 7, 2001**

REMARKS

Status of the Claims

By the foregoing amendments, Applicants seek to amend the section titled "Cross-Reference to Related Applications," in order to add the formerly missing application serial number, which was unavailable at the time of filing the application. Furthermore, by the foregoing amendments, Applicants seek to amend Claims 1-5 and 29-36, and Applicants seek entry of new Claims 37-42. The specific changes to the specification and the claims are shown above with insertions shown in underlined text and ~~deletions shown in strikethrough text~~. As evidenced below, these amendments do not introduce new matter into the application. Upon entry of the foregoing amendments, Claims 1-5 and 29-42 are pending in the application, with Claims 1 and 42 being the only independent claims.

Support for Amendments and New Claims

The specification has been amended in the paragraph beginning on page 1, line 6 to add the previously unknown serial number for the already-listed priority application. The filing date and attorney docket number were previously listed. Thus, no new matter is added.

Exemplary support for the amendments to Claim 1 is found in the specification at page 16, line 18 to page 17, line 10 (particularly lines 24-26; "[t]he method can include, for example, combining the T cell as described herein with a pharmaceutically acceptable adjuvant, carrier, diluent, excipient, and the like."); Claim 1 as filed, and in the specification at page 107, line 20 to page 108, line 15.

Exemplary support for amended Claims 2 and 3 is found at page 108, lines 3-4 ("These T cells can constitute a clone or a polyclonal population recognizing one or more epitopes."); in original Claims 2 and 3; and at page 16, line 18 to page 17, line 10.

Exemplary support for amended Claim 4 is found at page 107, lines 21-22 (Such T cells can be most readily obtained by *in vitro* immunization."); in original Claim 4; and at page 16, line 18 to page 17, line 10.

Exemplary support for amended Claim 5 is found at page 107, lines 27-28 ("Use of immunized donors, or patients themselves, as initial sources of T cells is also contemplated."); in original Claim 5; and at page 16, line 18 to page 17, line 10.

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Support for the amendments to Claims 29-36 is found, for example, throughout the specification, including at pages 16-17 and 107-108.

Exemplary support for new Claims 37 and 42 is found in original Claim 1, page 108, lines 3-4, and throughout the specification as filed.

Exemplary support for new Claims 38-39 is found in the specification at page 14, lines 23-26 ("The first antigen and the second antigen may be the same or different. Similarly, the first target cell and the second target cell may be the same or different.").

Exemplary support for new Claims 40-41 is found in the specification at page 108, lines 4-5.

Therefore, no new matter has been added by the amendments or by the addition of new Claims 37-42.

Priority

The priority claim was included with the application as filed, and included as much information as was available to Applicants at the time of filing. The previously unavailable information is now included. Therefore, the proper priority information for the instant application is as follows:

> This application is a continuation of U.S. Patent Application No. 10/005,905, (attorney docket number CTLIMM.021CP1) entitled EPITOPE SYNCHRONIZATION IN ANTIGEN PRESENTING CELLS, filed on November 7, 2001, now abandoned, which is a continuation-in-part of U.S. Patent Applications No. 09/561,074 entitled METHOD OF EPITOPE DISCOVERY, No. 09/560,465 entitled EPITOPE SYNCHRONIZATION IN ANTIGEN PRESENTING CELLS, No. 09/561,572 entitled EXPRESSION VECTORS ENCODING EPITOPES OF TARGET-ASSOCIATED ANTIGENS, and No. 09/561,571 entitled EPITOPE CLUSTERS, all filed April 28, 2000; and PCT Application Number PCT/US01/13806 entitled EPITOPE SYNCHRONIZATION IN ANTIGEN PRESENTING CELLS, filed April 27, 2001, all of which recited applications are incorporated herein by reference in their entirety.

Therefore, Applicants request that the priority claim be properly set according to the above information.

Discussion of Rejection under 35 U.S.C. § 112, Second Paragraph

Claims 1-5 and 29-36 were rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which

applicant regards as the invention. Specifically, the Examiner argued that recitation of "a first housekeeping epitope," "a first antigen," and "a first target cell," renders the claims indefinite because there is no indication of any second or additional elements in the claims.

Respectfully, Applicants assert that the claims are clear and definite with the objected-to recitation, particularly in view of the specification as filed. However, new Claim 37 has been added, and recites "second or additional elements related to the 'first' elements." Therefore, Applicants request withdrawal of the instant rejection.

Discussion of Rejection under 35 U.S.C. § 102

The Examiner rejected Claims 1-5, 29-36 under 35 U.S.C. § 102(b) as being anticipated by various references.

To be anticipatory under 35 U.S.C. § 102, a reference must teach each and every element of the claimed invention. *See Hybritech Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1379 (Fed. Cir. 1986). Respectfully, the cited references do not teach each and every element of the amended and new claims.

Zajac et al. Does Not Anticipate the Claims

Claims 1-5, 29-30 and 33-35 were rejected under § 102(b) as being anticipated by Zajac et al. ("Zajac") ("Generation of Tumoricidal Cytotoxic T Lymphocytes from Healthy Donors After *In Vitro* Stimulation with a Replication-Incompetent Vaccinia Virus Encoding Mart-1/Melan-A 27-35 Epitope," *Int. J. Cancer*, Vol. 71, pages 491-496, 1997). Zajac does not anticipate independent Claims 1 and 42 because it fails to teach each and every element of each of those claims.

Zajac was interested in active immunotherapy targeting tumor-associated antigens (TAAs). To that end, Zajac addresses the construction and evaluation of the immunogenicity of a replication deficient vaccinia virus expressing a tumor epitope (MART-1/Melan-A_{27-35}). Tumor-infiltrating lymphocytes (TILs) and peripheral-blood mononuclear cells (PBMCs) were stimulated with cells infected with the recombinant vaccinia vector, and tested to determine whether the infected cells were capable of inducing epitope specific CTLs. As part of the determination, to maximally expand epitope specific CTL, the lymphocytes were restimulated with peptide pulsed EBV-BL cells.

Zajac does not anticipate Claim 1, reciting a composition suitable for adoptive administration to an animal, because Zajac does not disclose a composition comprising a first isolated T cell in a pharmaceutically acceptable formulation, the formulation comprising a pharmaceutically acceptable carrier, adjuvant, diluent, or excipient.

This is not surprising as Zajac was not interested in a composition comprising, among other things, an isolated T cell, much less a T cell in combination with a pharmaceutically acceptable material. Rather Zajac sought to assess the ability of recombinant vaccinia viruses expressing a TAA to infect cells in order to induce TAA specific CTLs. Zajac manifests no interest in compositions suitable for adoptive administration, nor does Zajac disclose the claimed compositions. Furthermore, the assay protocols of Zajac utilize materials such as Epstein Barr Virus (EBV) transformed cells and fetal calf serum (FCS), which may not be pharmaceutically acceptable and likely render possible T cell compositions pharmaceutically unacceptable and unsuitable for adoptive administration to an animal. Furthermore, the protocols of Zajac use antibiotics, many of which are also unacceptable for pharmaceutical formulations. For these reasons Zajac does not teach all of the elements of Claim 1.

Zajac also does not anticipate new Claim 42 because Zajac does not disclose a composition suitable for adoptive administration comprising, among other things, a second isolated T cell population, wherein said second population expresses a . . . complex comprising a second housekeeping epitope. Zajac discloses T cells specific for a single epitope, MART-1/Melan-A_{27-35}, and therefore does not disclose each and every element of Claim 42.

Therefore, Zajac does not anticipate because it fails to teach each and every element of the independent claims.

Kittlesen et al. Does Not Anticipate the Claims

Claims 1-5, 29-30, 33-34 and 36 were rejected under § 102(b) as being anticipated by Kittlesen et al. ("Kittlesen ") ("Human Melanoma Patients Recognize an HLA-A1-Restricted CTL Epitope from Tyrosinase Containing Two Cysteine Residues: Implications for Tumor Vaccine Development," *J. Immunol.*, Vol. 160, pages 2099-2106, 1998). Kittlesen does not anticipate independent Claims 1 and 42 because it fails to teach each and every element of each of those claims.

Kittlesen involves the identification and optimization of tyrosinase epitopes capable of recognition on HLA-A1$^+$ target cells. The authors sought to identify non-HLA-A*0201 epitopes. In order to identify such epitopes, cells virally transformed to express tumor antigens were tested against HLA-A1 expressing CTL lines.

Kittlesen does not anticipate Claim 1, reciting a composition suitable for adoptive administration to an animal, because Kittlesen does not disclose a composition comprising a first isolated T cell in a pharmaceutically acceptable formulation, the formulation comprising a pharmaceutically acceptable carrier, adjuvant, diluent, or excipient. Again, this is not surprising in view of Kittlesen's objectives of identifying new epitope targets for active immunotherapy. Furthermore, the protocols of Kittlesen also use materials such as Epstein Barr Virus (EBV) transformed cells, Epstein Barr Virus containing supernatant, and fetal calf serum (FCS), which may not be pharmaceutically acceptable and likely, render possible T cell compositions pharmaceutically unacceptable and unsuitable for adoptive administration to an animal. Also, the protocols of Kittlesen use antibiotics, many of which are also unacceptable for pharmaceutical formulations. Kittlesen simply does not disclose the claimed composition. For these reasons Kittlesen does not teach all of the elements of Claim 1.

Kittlesen also does not anticipate new Claim 42 because Kittlesen does not disclose a composition suitable for adoptive administration comprising, among other things, both a first and a second isolated T cell population according to the claim. If Kittlesen discloses any compositions suitable for adoptive administration comprising isolated T cells, which it does not, such compositions only include a first isolated population, but not both a first and a second population. Thus, Kittlesen does not disclose each and every element of Claim 42.

For these reasons Kittlesen does not anticipate because it fails to teach each and every element of the independent claims.

Jäger et al. Does Not Anticipate the Claims

Claims 1-4, 29-32 and 35 were rejected under § 102(b) as being anticipated by Jäger et al. ("Jäger") ("Simultaneous Humoral and Cellular Immune Response Against Cancer-Testis Antigen NY-ESO-1: Definition of Human Histocompatibility Leukocyte Antigen (HLA)-A2-binding Peptide Epitopes," *J. Exp. Med.*, Vol. 187(2), pages 265-270, 1998). Zajac does not

anticipate independent Claims 1 and 42 because it fails to teach each and every element of each of those claims.

Jäger sought to more efficiently identify human tumor targets. Jäger purported to disclose the first conclusive demonstration of simultaneous antibody and CTL responses against a cancer-testis antigen in a single patient. Thus, Jäger suggested that its methodology can be used to analyze CTL reactivity against humoral (SEREX-defined antigens), and that serological methods may be used to monitor vaccine trials involving antigens that have the ability to elicit both humoral and cellular responses.

Jäger does not anticipate Claim 1, reciting a composition suitable for adoptive administration to an animal, because Jäger does not disclose a composition comprising a first isolated T cell in a pharmaceutically acceptable formulation, the formulation comprising a pharmaceutically acceptable carrier, adjuvant, diluent, or excipient. Again, this is not surprising in view of Jäger objectives of identifying tumor antigen that elicits both a humoral and a cellular immune response. The objective was not to generate a composition suitable for adoptive administration comprising a first isolated T cell and a pharmaceutically acceptable material. Furthermore, the protocols of Jäger also use materials such as Epstein Barr Virus (EBV) transformed cell lines and fetal calf serum (FCS), which may not be pharmaceutically acceptable and likely, render possible T cell compositions pharmaceutically unacceptable and unsuitable for adoptive administration to an animal. Also, the protocols utilize antibiotics (such as penicillin), many of which are also unacceptable for pharmaceutical formulations. Again, Jäger simply does not disclose the claimed composition. For these reasons Jäger does not teach all of the elements of Claim 1.

Jäger also does not anticipate new Claim 42 because Jäger does not disclose a composition suitable for adoptive administration comprising, among other things, both a first and a second isolated T cell population according to the claim. Thus, Jäger does not disclose each and every element of Claim 42.

Therefore, for the above reasons, Jäger does not anticipate because it fails to teach each and every element of the independent claims.

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Conclusion

Applicants have endeavored to address all of the Examiner's concerns as expressed in the outstanding Office Action. Accordingly, arguments in support of the patentability of the pending claim set are presented above. In light of the above amendments and remarks, reconsideration and withdrawal of the outstanding rejections is specifically requested. If the Examiner finds any remaining impediment to the prompt allowance of these claims that could be clarified with a telephone conference, the Examiner is respectfully requested to initiate the same with the undersigned.

Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. 11-1410.

Respectfully submitted,

KNOBBE, MARTENS, OLSON & BEAR, LLP

Dated: 9/15/04

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